L3 ANSWER 10 OF 10 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96006701 MEDLINE
DOCUMENT NUMBER: 96006701 PubMed ID: 7550366
TITLE: Polymorphisms of human Ah receptor gene are not involved in lung cancer.
AUTHOR: Kawajiri K; Watanabe J; Eguchi H; Nakachi K; Kiyohara C; Hayashi S
CORPORATE SOURCE: Department of Biochemistry, Saitama Cancer Center Research Institute, Japan.
SOURCE: PHARMACOGENETICS, (1995 Jun) 5 (3) 151-8.
Journal code: 9211735. ISSN: 0960-314X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19970203
Entered Medline: 19951024

AB The Ah receptor (Ahr) is a ligand-dependent transcription factor that positively regulates inducible expression of the CYP1A1 gene. Based on the sequence information of the human Ahr and the intron-**exon** junctions of the mouse counterpart, an analysis of single-strand conformational polymorphism (SSCP) was carried out to detect subtle base differences in the coding region of the gene among individuals. We found that the Ahr protein has at least two forms of variants in a Japanese gene pool, and that these variants can be ascribed to one amino acid replacement of Arg by Lys at codon 554. The frequencies of Arg-coded and Lys-coded alleles were 0.57 and 0.43, respectively. We found, however, that this germ line polymorphism of the Ahr gene did not show a significant association with aryl hydrocarbon hydroxylase (**AHH**) inducibility nor with lung cancer incidence.

L3 ANSWER 8 OF 10 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 96439142 MEDLINE
DOCUMENT NUMBER: 96439142 PubMed ID: 8841477
TITLE: A mutation in the p53 tumor suppressor gene of **AHH** -1 tk+/- human lymphoblastoid cells.
AUTHOR: Morris S M; Manjanatha M G; Shelton S D; Domon O E; McGarrity L J; Casciano D A
CORPORATE SOURCE: Division of Genetic Toxicology, Food and Drug Administration, Department of Health and Human Services, Jefferson, AR 72079, USA.. smorris@nctr.fda.gov
SOURCE: MUTATION RESEARCH, (1996 Sep 23) 356 (2) 129-34. Journal code: 0400763. ISSN: 0027-5107.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961120

AB Loss-of-function mutations in the p53 tumor suppressor gene result in an altered response to DNA-damaging agents. Included in the mutant p53 phenotype are the loss of the G1 checkpoint and delayed apoptotic cell death, characteristics we have consistently observed in the **AHH** -1 tk+/- cell line following exposure to DNA-damaging agents. In order to determine the functional status of p53 in the **AHH**-1 tk+/- cell line, molecular analysis (single-strand conformational polymorphism [SSCP] and sequence analysis) was performed on **exons** 5-9 of the p53 gene. In addition, the status of the p53 gene in the closely related lymphoblast line, MCL-5, which, in our hands, has a much higher spontaneous rate of apoptosis than **AHH**-1 tk+/-, was also determined by molecular analysis. Initial SSCP analysis of **AHH**-1 tk+/- revealed an abnormal migration pattern of **exon** 8 when compared to a wild-type control. Subsequent sequence analysis indicated that a base-pair substitution (CGG-->TGG) mutation had occurred at codon 282, a reported "hot spot' for 5-methylcytosine mutations in the human p53 gene. Neither SSCP nor sequence analysis of **exons** 5-9 of MCL-5 indicated any differences from wild-type DNA. These results suggest that the lack of a G1 arrest and the delayed entrance into apoptosis observed in chemically-exposed **AHH**-1 tk+/- cells are, at least partially, accounted for by a loss-of-function mutation in the p53 gene.

L3 ANSWER 4 OF 10 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001106027 MEDLINE
DOCUMENT NUMBER: 20564328 PubMed ID: 10956665
TITLE: **Aspartyl beta -hydroxylase** (Asph) and an evolutionarily conserved isoform of Asph missing the catalytic domain share **exons** with junctin.
AUTHOR: Dinchuk J E; Henderson N L; Burn T C; Huber R; Ho S P; Link J; O'Neil K T; Focht R J; Scully M S; Hollis J M; Hollis G F; Friedman P A
CORPORATE SOURCE: Department of Applied Biotechnology, DuPont Pharmaceuticals Research Laboratories, DuPont Pharmaceuticals Company, Experimental Station, Wilmington, Delaware 19880, USA.. joseph.e.dinchuk@dupontpharma.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Dec 15) 275 (50) 39543-54.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF289199; GENBANK-AF289200; GENBANK-AF289205; GENBANK-AF289206; GENBANK-AF289207; GENBANK-AF289208; GENBANK-AF289209; GENBANK-AF289210; GENBANK-AF289211; GENBANK-AF289212; GENBANK-AF289213; GENBANK-AF289214; GENBANK-AF289215; GENBANK-AF289486; GENBANK-AF289487; GENBANK-AF289488; GENBANK-AF289489; GENBANK-AF289490; GENBANK-AF289491; GENBANK-AF289492; GENBANK-AF289493; GENBANK-AF289494
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
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Entered Medline: 20010208

AB The mouse **aspartyl beta-hydroxylase** gene (Asph, BAH) has been cloned and characterized. The mouse BAH gene spans 200 kilobase pairs of genomic DNA and contains 24 **exons**. Of three major BAH-related transcripts, the two largest (6,629 and 4,419 base pairs) encode full-length protein and differ only in the use of alternative polyadenylation signals. The smallest BAH-related transcript (2,789 base pairs) uses an alternative 3' terminal **exon**, resulting in a protein lacking a catalytic domain. Evolutionary conservation of this noncatalytic isoform of BAH (humbug) is demonstrated in mouse, man, and Drosophila. Monoclonal antibody reagents were generated, epitope-mapped, and used to definitively correlate RNA bands on Northern blots with protein species on Western blots. The gene for mouse junctin, a calsequestrin-binding protein, was cloned and characterized and shown to be encoded from the same locus. When expressed in heart tissue, BAH/humbug preferably use the first **exon** and often the fourth **exon** of junctin while preserving the reading frame. Thus, three individual genes share common **exons** and open reading frames and use separate promoters to achieve differential expression, splicing, and function in a variety of tissues. This unusual form of **exon** sharing suggests that the functions of junctin, BAH, and humbug may be linked.

L3 ANSWER 3 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001106028 MEDLINE
DOCUMENT NUMBER: 20564329 PubMed ID: 11007777
TITLE: Molecular cloning, expression, functional characterization, chromosomal localization, and gene structure of junctate, a novel integral calcium binding protein of sarco(endo)plasmic reticulum membrane.
AUTHOR: Treves S; Feriotto G; Moccagatta L; Gambari R; Zorzato F
CORPORATE SOURCE: Departments of Anaesthesia and Research, Hebelstrasse 20, Kantonsspital, 4031 Basel, Switzerland.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Dec 15) 275 (50) 39555-68.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF306765
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB Screening a cDNA library from human skeletal muscle and cardiac muscle with a cDNA probe derived from junctin led to the isolation of two groups of cDNA clones. The first group displayed a deduced amino acid sequence that is 84% identical to that of dog heart junctin, whereas the second group had a single open reading frame that encoded a polypeptide with a predicted mass of 33 kDa, whose first 78 NH(2)-terminal residues are identical to junctin whereas its COOH terminus domain is identical to **aspartyl beta-hydroxylase**, a member of the alpha-ketoglutarate-dependent dioxygenase family. We named the latter amino acid sequence junctate. Northern blot analysis indicates that junctate is expressed in a variety of human tissues including heart, pancreas, brain, lung, liver, kidney, and skeletal muscle. Fluorescence in situ hybridization analysis revealed that the genetic loci of junctin and junctate map to the same cytogenetic band on human chromosome 8. Analysis of intron/**exon** boundaries of the genomic BAC clones demonstrate that junctin, junctate, and **aspartyl beta-hydroxylase** result from alternative splicing of the same gene. The predicted lumenal portion of junctate is enriched in negatively charged residues and is able to bind calcium. Scatchard analysis of equilibrium (45)Ca(2+) binding in the presence of a physiological concentration of KCl demonstrate that junctate binds 21.0 mol of Ca(2+)/mol protein with a k(D) of 217 +/- 20 microm (n = 5). Tagging recombinant junctate with green fluorescent protein and expressing the chimeric polypeptide in COS-7-transfected cells indicates that junctate is located in endoplasmic reticulum membranes and that its presence increases the peak amplitude and transient calcium released by activation of surface membrane receptors coupled to InsP(3) receptor activation. Our study shows that alternative splicing of the same gene generates the following functionally distinct proteins: an enzyme (**aspartyl beta-hydroxylase**), a structural protein of SR (junctin), and a membrane-bound calcium binding protein (junctate).

L3 ANSWER 1 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002204823 MEDLINE
DOCUMENT NUMBER: 21935316 PubMed ID: 11773073
TITLE: Absence of post-translational aspartyl beta-hydroxylation of epidermal growth factor domains in mice leads to developmental defects and an increased incidence of intestinal neoplasia.
AUTHOR: Dinchuk Joseph E; Focht Richard J; Kelley Jennifer A; Henderson Nancy L; Zolotarjova Nina I; Wynn Richard; Neff Nicola T; Link John; Huber Reid M; Burn Timothy C; Rupar Mark J; Cunningham Mark R; Selling Bernard H; Ma Jianhong; Stern Andrew A; Hollis Gregory F; Stein Robert B; Friedman Paul A
CORPORATE SOURCE: Bristol-Myers Squibb Pharma Research Labs, Inc., Wilmington, DE 19880-0400, USA.. joseph.dinchuk@bms.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Apr 12) 277 (15) 12970-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020409
Last Updated on STN: 20020517
Entered Medline: 20020516

AB The BAH genomic locus encodes three distinct proteins: junctin, humbug, and BAH. All three proteins share common **exons**, but differ significantly based upon the use of alternative terminal **exons**. The biological roles of BAH and humbug and their functional relationship to junctin remain unclear. To evaluate the role of BAH in vivo, the catalytic domain of BAH was specifically targeted such that the coding regions of junctin and humbug remained undisturbed. BAH null mice lack measurable BAH protein in several tissues, lack **aspartyl beta-hydroxylase** activity in liver preparations, and exhibit no hydroxylation of the epidermal growth factor (EGF) domain of clotting Factor X. In addition to reduced fertility in females, BAH null mice display several developmental defects including syndactyly, facial dysmorphology, and a mild defect in hard palate formation. The developmental defects present in BAH null mice are similar to defects observed in knock-outs and hypomorphs of the Notch ligand Serrate-2. In this work, beta-hydroxylation of Asp residues in EGF domains is demonstrated for a soluble form of a Notch ligand, human Jagged-1. These results along with recent reports that another post-translational modification of EGF domains in Notch gene family members (glycosylation by Fringe) alters Notch pathway signaling, lends credence to the suggestion that aspartyl beta-hydroxylation may represent another post-translational modification of EGF domains that can modulate Notch pathway signaling. Previous work has demonstrated increased levels of BAH in certain tumor tissues and a role for BAH in tumorigenesis has been proposed. The role of hydroxylase in tumor formation was tested directly by crossing BAH KO mice with an intestinal tumor model, APCmin mice. Surprisingly, BAH null/APCmin mice show a statistically significant increase in both intestinal polyp size and number when compared with BAH wild-type/APCmin controls. These results suggest that, in contrast to expectations, loss of BAH catalytic

activity may promote tumor formation.